and calculate the cefaclor content as follows:

(*a*) *Preparation of working standard solution.* Dissolve and dilute an accurately weighed portion of the cefaclor working standard in sufficient 0.1*M* potassium phosphate buffer, pH 4.5 (as described in §436.101(a)(4) of this chapter) to obtain a concentration of 1 milligram of cefaclor per milliliter.

(*b*) *Preparation of sample solution.* Dissolve an accurately weighed portion of the sample in sufficient 0.1*M* potassium phosphate buffer, pH 4.5 (as described in §436.101(a)(4) of this chapter) to obtain a concentration of 1 milligram of cefaclor per milliliter.

(*c*) *Calculations.* Calculate the cefaclor content in micrograms per milligram as follows:

$$\text{Micrograms of cefaclor per milligram of sample} = \frac{A_u \times P_a}{A_s \times W_u}$$

where:

A_u = Absorbance of sample solution;
P_a = Potency of working standard solution in micrograms per milliliter;
A_s = Absorbance of working standard solution;
W_u = Milligrams of sample per milliliter of sample solution.

(2) *Moisture.* Proceed as directed in §436.201 of this chapter.

(3) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous suspension containing 25 milligrams per milliliter.

(4) *Identity.* Proceed as directed in §436.211 of this chapter, using the sample preparation described in paragraph (b)(2) of that section.

(5) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[46 FR 3832, Jan. 16, 1981]

§442.6 Cefadroxil monohydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefadroxil monohydrate is 7-[D-2-amino-2(*p*-hydroxyphenyl)acetamido] - 3 - methyl - 8 - oxo- 5-thia-1-azabicyclo[4.2.0] oct-2-ene-2-carboxylic acid monohydrate. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms and not more than 1,050 micrograms of cefadroxil per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not less than 4.2 percent and not more than 6.0 percent.

(iv) Its pH in an aqueous solution containing 50 milligrams per milliliter is not less than 4.0 and not more than 6.0.

(v) When calculated on an anhydrous basis, its absorptivity at 264 nanometers is not less than 95 percent and not more than 104 percent of that of the cefadroxil standard similarly treated and corrected for potency.

(vi) It passes the identity test.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, absorptivity, identity, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 20 micrograms of cefadroxil per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay for cefadroxil.* Proceed as directed in §442.40(b)(1)(ii) of this chapter, except prepare the working standard and sample solutions and calculate the potency of the sample as follows:

(*a*) *Preparation of working standard solutions.* Dissolve and dilute an accurately weighed portion of the cefadroxil working standard in sufficient distilled water to obtain a stock

solution of convenient concentration. Further dilute an aliquot of this solution with distilled water to a concentration of 1 milligram of cefadroxil per milliliter.

(*b*) *Preparation of sample solutions.* Dissolve an accurately weighed portion of the sample in sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of this solution with distilled water to a concentration of 1 milligram of cefadroxil per milliliter (estimated).

(*c*) Calculate the potency of the sample in micrograms per milligram as follows:

$$\frac{\text{Micrograms of cefadroxil per milligram of sample}}{} = \frac{A_u \times P_a \times 100}{A_s \times W_u \times (100 - m)}$$

where:

A_u=Absorbance of sample solution;
P_a=Potency of working standard solution in micrograms per milliliter;
A_s=Absorbance of working standard solution;
W_u=Milligrams of sample per milliliter of sampe solution;
m=Percent moisture in sample.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 50 milligrams per milliliter.

(5) *Absorptivity.* Determine the absorbance of the sample and standard solutions in the following manner: Dissolve accurately weighed portions of approximately 50 milligrams each of the sample and standard in 250 milliliters of distilled water. Transfer a 10-milliliter aliquot to a 100-milliliter volumetric flask and dilute to volume with distilled water. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of each solution at 264 nanometers. Determine the percent absorptivity of the sample relative to the absorptivity of the standard using the following calculations:

Percent relative absorptivity=[Absorbance of sample × milligrams standard × potency of standard in micrograms per milligram × 10]/[Absorbance of standard × milligrams sample × (100-*m*)]

where:

m=Percent moisture in the samples.

(6) *Identity.* Using the sample and working standard solutions prepared as described in paragraph (b)(5) of this section and a suitable spectrophotometer, record the ultraviolet spectrum from 220 to 340 nanometers. The spectrum of the sample compares qualitatively with that of the cefadroxil working standard.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[43 FR 20977, May, 16, 1978; 43 FR 27180, June 23, 1978, as amended at 50 FR 19919, May 13, 1985]

§ 442.7 Cefadroxil hemihydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefadroxil hemihydrate is 7-[D-2-amino-2(*p*-hydroxyphenyl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid hemihydrate. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms and not more than 1,050 micrograms of cefadroxil activity per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not less than 2.4 percent and not more than 4.5 percent.

(iv) The pH of an aqueous solution containing 50 milligrams per milliliter is not less than 4.0 and not more than 6.0.

(v) When calculated on an anhydrous basis, its absorptivity at 264 nanometers is not less than 95 percent and not more than 104 percent of that of the cefadroxil standard similarly treated and corrected for potency.

(vi) It passes the identity test.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for cefadroxil potency, moisture, pH, absorptivity, identity, and crystallinity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and